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In-hospital and thirty-day outcomes of the SAPIEN 3 Ultra balloon-expandable transcatheter aortic valve: the S3U registry



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KEYWORDS

- aortic stenosis
- femoral
- miscellaneous
- TAVI

Abstract

Aims: The aim of this study was to evaluate 30-day safety and efficacy outcomes of transcatheter aortic valve implantation (TAVI) performed with the SAPIEN 3 Ultra system.

Methods and results: The S3U registry is a physician-led, post-approval, multicentre, observational registry of transfemoral TAVI with the SAPIEN 3 Ultra. New features include an improved sealing skirt, a 14 Fr expandable sheath and a new delivery catheter. Overall, 139 consecutive patients at nine participating centres were enrolled. Mean age was 81.4 ± 8.3 years, average STS score $3.8 \pm 2.4\%$. The vast majority (97.2%) underwent TAVI with local anaesthesia (28.8%) or conscious sedation (68.3%). Balloon predilatation was performed in 30 patients (21.6%), post-dilatation in three (2.2%). In-hospital, there were no cases of death, stroke, or conversion to open heart surgery. Major vascular complications occurred in three patients (2.2%), as well as major or life-threatening bleedings in three patients (2.2%). There were two moderate (1.4%) and no moderate/severe paravalvular leaks. Median length of stay after TAVI was three days (IQR 3-5 days). At 30 days, there were no deaths, MI, or strokes, and the incidence of new permanent pacemaker implantation was 4.4%.

Conclusions: This first multicentre international experience of transfemoral TAVI with the SAPIEN 3 Ultra transcatheter heart valve shows good in-hospital and 30-day clinical outcomes.

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Abbreviations

EuroSCORE	European System for Cardiac Operative Risk Evaluation
IPE	initial product evaluation
PPM	permanent pacemaker
PVL	paravalvular leak
SAVR	surgical aortic valve replacement
S3U	SAPIEN 3 Ultra
STS PROM	Society of Thoracic Surgeons predicted risk of mortality
TAVI	transcatheter aortic valve implantation
VARC-2	Valve Academic Research Consortium-2

Introduction

Transcatheter aortic valve implantation (TAVI) represents an alternative to surgical aortic valve replacement (SAVR) for elderly patients with severe aortic stenosis (AS). Randomised clinical trials have demonstrated the superiority of TAVI over medical therapy in patients at prohibitive surgical risk, and equivalence or superiority over SAVR for all other surgical risk categories¹⁻⁷. The field of TAVI is rapidly evolving, with major refinements in technology, procedural techniques, patient selection and biomedical engineering. With the development of improved devices, new approaches and new implantation strategies, TAVI has become much simpler and safer. The first transcatheter heart valve device implanted in man in 2002 was a balloon-expandable device⁸. Since then, three further device iterations have been released and approved for clinical use by Edwards Lifesciences (Irvine, CA, USA): the SAPIEN⁹, the SAPIEN XT¹⁰, and the SAPIEN 3¹¹. Changes have included innovations in the valve, the delivery system and the introducer sheath. The recently released SAPIEN 3 Ultra (Edwards Lifesciences) is the latest development whose features include an improved sealing skirt, a lower profile, and a simplified delivery catheter; it has gained approval for commercial use in Europe and the USA. To date, there have been no reports documenting clinical experience with the SAPIEN 3 Ultra.

We herein report the 30-day outcomes of the S3U registry, a physician-led, post-approval multicentre, real-world observational registry of transfemoral TAVI with the SAPIEN 3 Ultra device.

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Methods

STUDY DESIGN AND PATIENT POPULATION

The SAPIEN 3 Ultra received CE mark approval in November 2018. Since then, an initial product evaluation (IPE) phase has been launched, with a limited product release in selected centres across Europe. The IPE was terminated in December 2018. Concurrently, we designed a physician-led, international, multicentre, prospective registry aimed at collecting clinical, echocardiographic, procedural and outcome data of the first consecutive transfemoral SAPIEN 3 Ultra procedures performed within the IPE phase and up to February 2019. In total, nine centres participated in the study. The indication for TAVI was determined by a Heart Team. The selection of the SAPIEN 3 Ultra was based on labelled indications

and the final decision was then left to the operators. The manufacturer of the SAPIEN 3 Ultra, Edwards Lifesciences, had no role in data collection, analysis, or manuscript drafting and did not provide any financial support for the study.

THE SAPIEN 3 ULTRA DEVICE (Figure 1)

The SAPIEN 3 Ultra retains the SAPIEN 3 cobalt-chromium alloy frame, with a low delivery profile and high radial strength. The SAPIEN 3 Ultra characteristics and differences compared to the SAPIEN 3 are shown in **Figure 1**. Briefly, the most important changes are related to the outer skirt made from a textured polyethylene terephthalate (PET) and 40% higher than that of the SAPIEN 3 for a better final sealing. The SAPIEN 3 Ultra is available in three sizes (20, 23 and 26 mm), whereas the 29 mm valve is the SAPIEN 3 mounted on the Ultra delivery system. The delivery system was also modified with on-balloon valve crimping to streamline the procedure, eliminating the need for valve alignment and flex catheter retraction steps. The crossing profile is lower thanks to smooth tip-to-valve transition and to a shorter tapered distal tip. Finally, the Axela sheath has replaced the eSheath with new features. It is a 14 Fr expandable sheath for all valve sizes, including the 29 mm SAPIEN 3. It has a hydrophilic coating for smooth insertion, tracking and removal. The specific design allows transient expansion and active contraction and, by means of a seamless design, it maintains optimal haemostasis throughout the procedure.

DEFINITIONS AND OUTCOMES

All patients had symptomatic severe native AS defined by standard criteria. Peripheral artery disease (PAD) included a history of intermittent claudication, previous peripheral vascular treatment or documented peripheral arterial stenosis greater than 50%. Chronic obstructive pulmonary disease was identified by forced expiratory volume in one second <1 litre or long-term use of bronchodilators, steroids or oxygen for lung disease. Chronic kidney disease (CKD) was identified by a glomerular filtration rate (GFR) <60 ml/min calculated by the Cockcroft-Gault formula. The logistic EuroSCORE (European System for Cardiac Operative Risk Evaluation), the EuroSCORE II and the Society of Thoracic Surgeons predicted risk of mortality (STS PROM) score were reported as part of a multiparametric evaluation^{12,13}. TAVI procedures were performed as per the standard practice of each centre. There was no standardisation of post-procedural antithrombotic therapy. The primary objective of the study was to evaluate post-procedural and 30-day safety and efficacy outcomes. All end-points were defined according to the Valve Academic Research Consortium-2 (VARC-2) criteria¹⁴. The main outcomes of interest were device success, all-cause death, cardiac death, stroke, vascular complications, bleeding, new permanent pacemaker insertion and acute kidney injury. Implant success was defined as only one valve implanted in the proper anatomical location, and device success according to VARC-2 criteria. All events and values collected are site-reported. The 30-day outcome was obtained through an outpatient clinic visit or telephone contact.

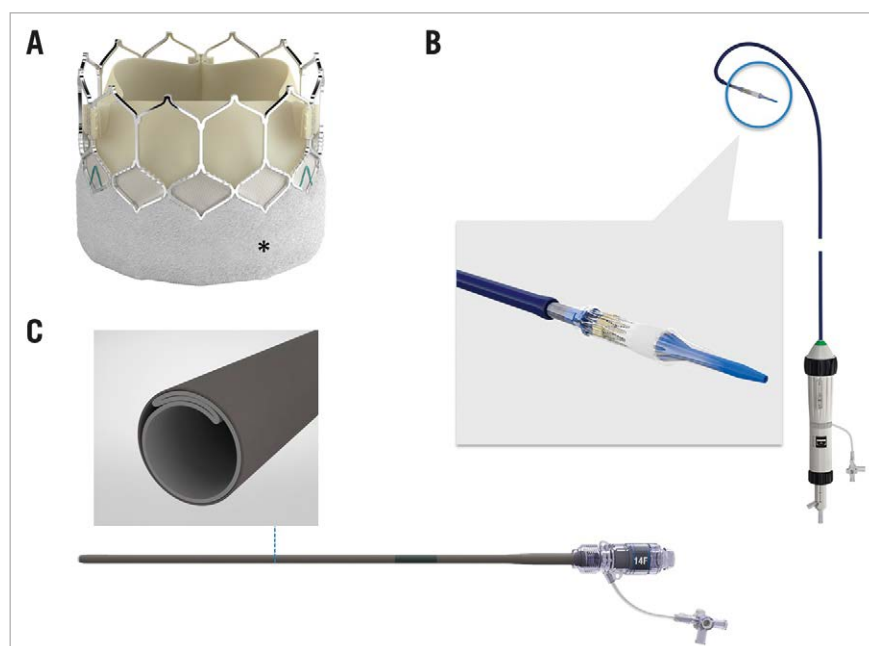


Figure 1. The SAPIEN 3 Ultra device. The SAPIEN 3 Ultra presents a number of important innovations in comparison with the SAPIEN 3 device, that involve the valve, the delivery system, and the introducer sheath. A) The valve retains the SAPIEN 3 frame and bovine pericardial leaflets, whereas the outer skirt (asterisk) is made of textured PET, different from the fabric seal of the SAPIEN 3 and around 40% higher. B) The Ultra delivery system. Highlighted, the new balloon re-designed to allow on-balloon valve crimping, obviating the need for valve alignment and pusher retraction before valve release. The distal end presents a smoother tip-to-valve transition and a shorter tapered distal tip. C) The Axela sheath: 14 Fr expandable sheath compatible with all valve sizes, engineered to allow transient expansion and active contraction (square box), with hydrophilic coating and a seamless design.

STATISTICAL ANALYSIS

Descriptive statistics are reported. Continuous variables were expressed as mean±standard deviation (SD), or median and inter-quartile range (IQR) when appropriate, and categorical variables as counts and percentages. All analyses were performed with the SAS 9.3 system (SAS Institute, Cary, NC, USA). Prospective TAVI databases were approved by the local ethics committee at each participating centre, and patients signed written informed consent for enrolment in the registry where required. The study protocol is in accordance with the Declaration of Helsinki. For the UK, data were collected as part of a mandatory UK national cardiac audit and all patient identifiable fields were removed before analysis. The study complies with section 251 of the National Health Service Act 2006. Ethical approval was not required under research governance arrangements for analyses.

Results

During the study period, 139 consecutive patients underwent transfemoral TAVI with the SAPIEN 3 Ultra at participating centres and were enrolled in the registry. Baseline characteristics are reported in **Table 1** and **Table 2**. Mean age was 81.4±8.3 years, 54.5% were female and the average STS score was 3.8±2.4%. The vast majority of subjects (97.2%) underwent TAVI with local anaesthesia (28.8%) or by conscious sedation (68.3%) (**Table 3**). The new SAPIEN 3 Ultra valves 20, 23 or 26 mm were used in

118 patients (84.9%), and the SAPIEN 3 29 mm with the Axela sheath and the Ultra delivery system in 21 (15.1%). In one patient, the 23 mm valve got stuck in the sheath and could not be further advanced, requiring a sheath exchange and replacement of the valve with a new one. The procedure ended successfully but there was a flow-limiting dissection of the iliac artery that had to be fixed with a peripheral stent from the contralateral femoral artery. Re-analysis of the angio-CT scan confirmed a minimal diameter of 5.5 mm without relevant calcifications or tortuosity at the site of sheath kinking. Most of the valves were implanted without balloon predilatation (78.4%). Post-dilatation was performed in three cases (2.2%). Mean procedural duration, from entrance to exit from the catheterisation laboratory, was 121±47 minutes. Implant success was 100%, and device success according to the VARC-2 definition was 97.8%; there were two cases (1.4%) with moderate paravalvular leak (PVL), and one case (0.7%) with a mean final gradient >20 mmHg and patient-prosthesis mismatch (aortic valve area [AVA] <0.65 cm²/m²) with a 20 mm device. In-hospital, there were no cases of death, stroke, or conversion to open heart surgery. The rate of new permanent pacemaker implantation to discharge was 2.2%. Major vascular complications occurred in three patients (2.2%), and major or life-threatening bleedings in three patients (2.2%). Valve haemodynamics and incidence of PVL are shown in **Figure 2**. Mean transvalvular gradients were 19±6 mmHg for the 20 mm device, 12±4 mmHg for the 23 mm,

Table 1. Baseline characteristics.

	(n=139)
Demographics	
Age, yrs	81.4±8.3
Female gender, n (%)	77 (55.4)
Body mass index, kg/m ²	27.3±4.6
Risk factors	
Diabetes, n (%)	31 (22.3)
Hypertension, n (%)	125 (89.9)
Dyslipidaemia, n (%)	82 (59.0)
Smoking	14 (10.1)
Clinical history	
Previous myocardial infarction, n (%)	25 (18.0)
Previous PCI, n (%)	46 (33.1)
Previous CABG, n (%)	9 (6.5)
Previous AVR, n (%)	0 (0.0)
Previous stroke, n (%)	11 (7.9)
Permanent pacemaker, n (%)	10 (7.2)
Comorbidities	
CKD, n (%)	87 (62.6)
Dialysis, n (%)	2 (1.4)
COPD, n (%)	20 (14.4)
PAD, n (%)	13 (9.5)
CVD, n (%)	11 (7.9)
Atrial fibrillation, n (%)	35 (25.2)
Neurologic dysfunction, n (%)	6 (4.3)
Clinical presentation	
Dyspnoea, n (%)	138 (99.3)
NYHA I-II	56 (40.3)
NYHA III-IV	82 (59.0)
Stable angina, n (%)	15 (10.8)
Syncope, n (%)	14 (10.1)
Pulmonary hypertension*, n (%)	9 (6.5)
Surgical risk	
STS PROM, %	3.8±2.4
Logistic EuroSCORE, %	14.0±11.5
EuroSCORE II, %	4.6±4.7
Severe liver disease, n (%)	5 (3.6)
Hostile thorax, n (%)	1 (0.7)
Porcelain aorta, n (%)	11 (7.9)
ECG	
LBBB	8 (5.8)
RBBB	10 (7.2)
1 st degree AVB	12 (8.6%)
*Systolic pulmonary arterial pressure >60 mmHg. AVB: atrioventricular block; AVR: aortic valve replacement; CABG: coronary artery bypass graft; CKD: chronic kidney disease (GFR <60 ml/min); COPD: chronic obstructive pulmonary disease; CVD: cerebrovascular disease; EuroSCORE: European System for Cardiac Operative Risk Evaluation; LBBB: left bundle branch block; PAD: peripheral artery disease; PCI: percutaneous coronary intervention; RBBB: right bundle branch block; STS PROM: Society of Thoracic Surgeons predicted risk of mortality	

Table 2. Echocardiography.

	Baseline (n=139)	Discharge (n=139)
Echocardiography		
AVA, cm ²	0.6±0.2	1.6±0.4
AVAi, cm ² /m ²	0.4±0.1	1.0±0.3
Mean transvalvular gradient, mmHg	46.3±13.8	11.6±4.3
Max transvalvular gradient, mmHg	75.4±21.4	21.3±6.8
LVEF, %	57.9±10.6	58.1±10.3
LVEF <30%, n (%)	3 (2.2)	2 (1.4)
Mitral regurgitation, n (%)		
None	21 (15.1)	41 (29.5)
Mild	71 (51.1)	60 (43.2)
Moderate	31 (22.3)	15 (10.8)
Moderate-to-severe	4 (2.9)	3 (2.2)
Severe	4 (2.9)	3 (2.2)
Aortic regurgitation, n (%)		
None	49 (35.3)	123 (88.5)
Mild	63 (45.3)	14 (10.1)
Moderate	17 (12.2)	2 (1.4)
Moderate-to-severe	1 (0.7)	0 (0.0)
Severe	3 (2.2)	0 (0.0)
AVA: aortic valve area; AVAi: indexed AVA; LVEF: left ventricular ejection fraction		

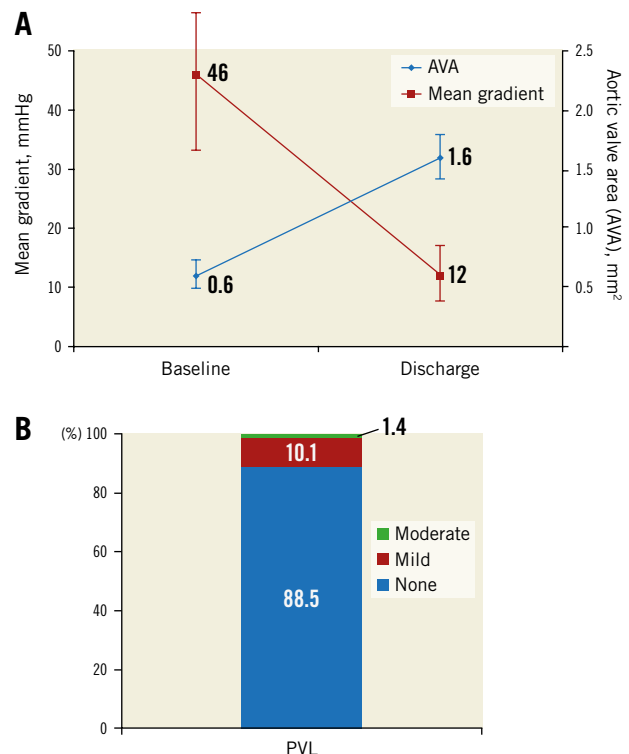


Figure 2. Haemodynamics and paravalvular regurgitation (PVL).
 A) Aortic valve area (AVA) before and after transcatheter aortic valve implantation at echocardiography. B) PVL grade before hospital discharge.

Table 3. Procedural, in-hospital and 30-day outcomes.

Patients (n=139)	
Anaesthesia/sedation status	
Stand-alone local anaesthesia, n (%)	40 (28.8)
Conscious sedation, n (%)	95 (68.3)
General anaesthesia, n (%)	4 (2.9)
Valve size, n (%)	
20 mm, n (%)	5 (3.6)
23 mm, n (%)	60 (43.2)
26 mm, n (%)	53 (38.1)
29 mm, n (%)	21 (15.1)
Predilatation	30 (21.6)
Device success, n (%)	136 (97.8)
Valve malposition, n (%)	0 (0.0)
Need for second valve, n (%)	0 (0.0)
Conversion to open surgery, n (%)	0 (0.0)
Cardiac tamponade, n (%)	0 (0.0)
Coronary occlusion, n (%)	0 (0.0)
Annulus rupture, n (%)	0 (0.0)
In-hospital	
All-cause death, n (%)	0 (0.0)
Acute myocardial infarction, n (%)	0 (0.0)
Stroke, n (%)	0 (0.0)
Vascular complications	
Major vascular complications, n (%)	3 (2.2)
Minor vascular complications, n (%)	15 (10.8)
Bleeding, n (%)	
Life-threatening or disabling bleeding	1 (0.7)
Major bleeding	2 (1.4)
Minor bleeding	6 (4.3)
Acute kidney injury, n (%)	
Class 1	4 (2.9)
Class 2	0 (0.0)
Class 3	5 (3.6)
New permanent pacemaker, n (%)	3 (2.2)
New atrial fibrillation, n (%)	5 (3.6)
30-day outcome	
All-cause death, n (%)	0 (0.0)
Cardiovascular death, n (%)	0 (0.0)
Stroke, n (%)	0 (0.0)
Re-hospitalisation for CHF, n (%)	3 (2.2)
New permanent pacemaker, n (%)	3 (2.2)
CHF: congestive heart failure	

11±4 mmHg for the 26 mm, and 10±4 mmHg for the 29 mm. In one patient, a focal leaflet thickening suggestive of thrombosis was detected at post-procedural echocardiography, without affecting transvalvular gradients. The thickening resolved after 24 hours of full anticoagulation and the patient was discharged with a mean

gradient of 10 mmHg. The median length of stay after TAVI was three days (IQR 3-5 days), and total hospitalisation was four days (IQR 2-7 days). At 30 days (**Table 3, Figure 3**), there were no deaths, MI, or strokes. Antithrombotics at discharge were dual antiplatelets in 58%, single antiplatelets in 7%, and oral anticoagulation in 35% (20% direct anticoagulants, in 10% combined with a single antiplatelet). Three additional patients required a new permanent pacemaker after discharge, with an overall 30-day incidence of 4.4%, and three patients were re-admitted because of congestive heart failure (CHF) (two paroxysmal atrial fibrillation [AF] with high heart rate, and one obese and severely hypertensive patient who inappropriately reduced diuretics). In all patients who were re-admitted, echocardiography showed a well-functioning prosthesis.

The present patient population was compared with a control population composed of 139 consecutive patients treated with the SAPIEN 3 in the period immediately preceding the introduction of the Ultra system. The results are shown in **Supplementary Table 1** and **Supplementary Table 2**. Briefly, patients treated with the Ultra were more frequently female with an overall lower surgical risk (e.g., STS PROM 3.8±2.4% vs 6.1±5.0%). There were no significant differences regarding in-hospital and 30-day outcomes.

Discussion

The current analysis reports for the first time on procedural and clinical outcomes in a consecutive series of patients undergoing transfemoral TAVI with the SAPIEN 3 Ultra in the prospective, international, multicentre S3U registry. The main findings are the following. 1) Device success was observed in 98% of the cases. 2) In-hospital, there were no cases of death, stroke or conversion to open heart surgery. The PPM rate, major vascular complications and severe bleeding were below 3%, and PVL below 2% (none >moderate). 3) Valve haemodynamics seem comparable to the SAPIEN 3. 4) These results were maintained at 30 days with the final incidence of new PPM being 4.4%. In addition, the rate of post-dilatation was low, compared with modern series, at 2.2%, perhaps indicating the better sealing characteristics of the improved PET skirt.

The technical changes of the SAPIEN 3 Ultra compared to the SAPIEN 3 were aimed at streamlining the procedure, making it safer, expanding the number of patients treatable using the transfemoral access and, most importantly, reducing the incidence of PVL. Our initial experience, with strict on-label use of the SAPIEN 3 Ultra, confirms these expectations in terms of both early procedural and clinical results. Of note, general anaesthesia was not needed in 97.2%, balloon predilatation was performed in a minority of patients, and the median hospital length of stay after TAVI was three days. Most importantly, we report an exceptionally low incidence of all major complications both in-hospital and at 30 days that parallels those reported by Waksman and colleagues with the use of the SAPIEN 3 in low-risk patients¹⁵. However, we enrolled older patients (on average +8 years) and, differently from the low-risk TAVR study, we included patients across all risk categories.

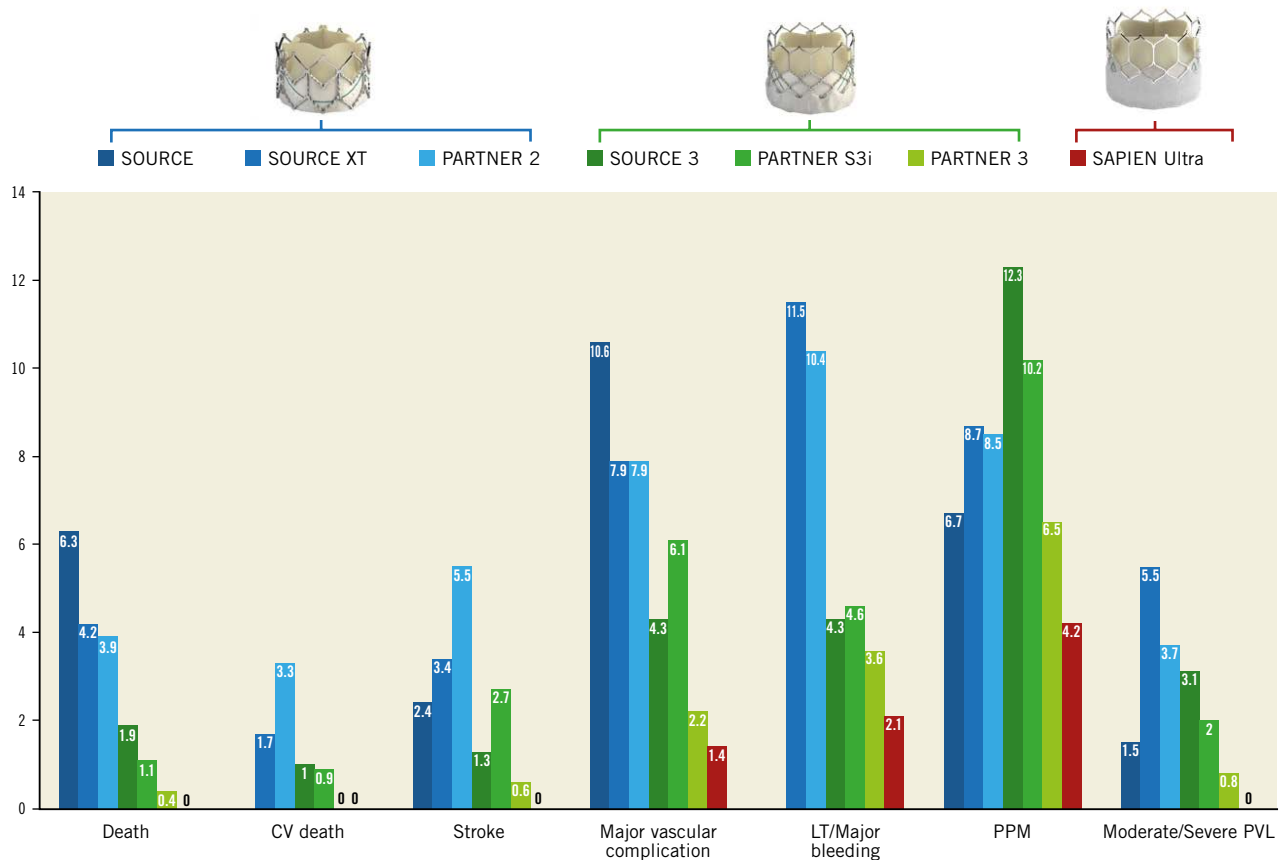


Figure 3. Thirty-day clinical outcomes. Thirty-day results of the SAPIEN 3 Ultra (S3U) registry in comparison with the main trials and registries of the SAPIEN transcatheter heart valve family.

There was, however, one case with a small kinking of the sheath that was not visible on angiography but precluded valve advancement, finally causing a minor vascular complication. Whether this could be attributed to the play of chance or to a somewhat minor resistance to compression of the Axela sheath cannot be inferred from our data. After completion of this study, other similar cases have been reported worldwide. In addition, a few cases of unexplained balloon rupture during valve implant have been reported which have resulted in significant difficulty retrieving the valve into the catheter and withdrawing the system from the patient. In some cases, this was associated with vascular injury, bleeding, or need for surgical intervention, prompting the manufacturer to issue a Field Safety Notice and, later on, the US Food and Drug Administration (FDA) to issue a class I recall of the SAPIEN 3 Ultra delivery system¹⁶. Following these events, the company is now supporting the use of the SAPIEN 3 Ultra with the Edwards Commander delivery system through the 14 Fr expandable eSheath.

In contrast with previous studies which have observed a higher rate of pacemaker requirement with the SAPIEN 3^{4,11,17} compared to the SAPIEN XT trials^{2,10}, the rate of PPM implantation in our study was low at 4.4% to 30 days. The reasons for this observation are speculative and may have occurred by chance or be explained by the small cohort size. Our patient population presented a low

rate of right bundle branch block (RBBB) or conduction disturbances at baseline. However, it is possible that the low rate of pre-dilatation, afforded by the lower crossing profile of the device and the low rate of post-dilatation, due to the improved sealing skirt reducing PVL, may have been contributory factors.

Limitations

This study presents some limitations that should be acknowledged. This is a relatively small series of SAPIEN 3 Ultra-treated patients performed by very experienced operators working in high-volume centres. Second, outcomes were self-reported by participating centres in the absence of a clinical events committee, and there was no core lab evaluation of echocardiographic results. While hard clinical endpoints such as mortality, stroke and major bleedings can be considered highly reliable, echocardiography and haemodynamics could suffer from inter-centre differences in evaluation and reporting. Overall, the external validity of these results should be evaluated in larger studies. Importantly, however, our results were obtained in the learning phase of the new device for all operators, confirming the safety and the efficacy of the SAPIEN 3 Ultra even under these circumstances. The comparison with previous-generation devices (**Figure 3**) is provided only for descriptive purposes and has no scientific validity. In fact, we cannot assume

that the improved outcomes are due only to the device because the time period is different, and it is well established that outcomes are improving due to increased experience. Finally, in the present study, all cases were performed with the Axela sheath and the Ultra delivery system. After identification of potential issues with both devices, in most centres the SAPIEN 3 Ultra valve is now implanted using the SAPIEN 3 delivery kit consisting of the eSheath and the Commander delivery system. Although it is reasonable to assume consistent results with the latter combination, further testing is needed to confirm this hypothesis.

Conclusions

This first multicentre experience of patients treated by transfemoral TAVI with strict on-label use of the new SAPIEN 3 Ultra transcatheter heart valve shows good in-hospital and 30-day clinical outcomes, confirming that refinements in technology and biomedical engineering may simplify and improve overall TAVI results.

Impact on daily practice

Transcatheter aortic valve implantation (TAVI) represents an alternative to surgical aortic valve replacement (SAVR) for elderly patients with severe aortic stenosis (AS) irrespective of surgical risk. TAVI devices are constantly being refined to address shortcomings of previous generations. This investigator-driven multicentre international study is the first to evaluate in-hospital and 30-day clinical outcomes associated with the latest-generation balloon-expandable transcatheter heart valve of the SAPIEN family, the SAPIEN 3 Ultra, demonstrating effective reduction of short-term complications and good clinical results.

Conflict of interest statement

F. Saia reports receiving consulting fees from Abbott Vascular, Eli Lilly, AstraZeneca, St. Jude Medical, and speaker's fees from Abbott Vascular, Eli Lilly, AstraZeneca, St. Jude Medical, Terumo, Biosensors, Edwards, and Boston Scientific, and personal fees from Edwards, outside the submitted work. G. Tarantini reports speaker's fees from Abbott Vascular, Edwards, Boston Scientific, and Medtronic. S.N. Doshi has received consulting fees from Medtronic, Edwards Lifesciences and Boston Scientific, and is a proctor for Edwards Lifesciences. M. Laine reports consulting fees from Boston Scientific, Medtronic and Edwards Lifesciences. F.L. Ribichini is a proctor for Edwards and reports personal fees from Edwards, outside the submitted work. T. Palmerini reports personal fees from Edwards, outside the submitted work. The other authors have no conflicts of interest to declare.

References

1. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S; PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010;363:1597-607.

2. Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, Thourani VH, Tuzcu EM, Miller DC, Herrmann HC, Doshi D, Cohen DJ, Pichard AD, Kapadia S, Dewey T, Babaliaros V, Szeto WY, Williams MR, Kereiakes D, Zajarias A, Greason KL, Whisenant BK, Hodson RW, Moses JW, Trento A, Brown DL, Fearon WF, Pibarot P, Hahn RT, Jaber WA, Anderson WN, Alu MC, Webb JG; PARTNER 2 Investigators. Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients. *N Engl J Med*. 2016;374:1609-20.
3. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock SJ; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med*. 2011;364:2187-98.
4. Mack MJ, Leon MB, Thourani VH, Makkar R, Kodali SK, Russo M, Kapadia SR, Malaisrie SC, Cohen DJ, Pibarot P, Leipsic J, Hahn RT, Blanke P, Williams MR, McCabe JM, Brown DL, Babaliaros V, Goldman S, Szeto WY, Genereux P, Pershad A, Pocock SJ, Alu MC, Webb JG, Smith CR; PARTNER 3 Investigators. Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients. *N Engl J Med*. 2019;380:1695-705.
5. Adams DH, Popma JJ, Reardon MJ, Yakubov SJ, Coselli JS, Deeb GM, Gleason TG, Buchbinder M, Hermiller J Jr, Kleiman NS, Chetcuti S, Heiser J, Merhi W, Zorn G, Tadros P, Robinson N, Petrossian G, Hughes GC, Harrison JK, Conte J, Maini B, Mumtaz M, Chenoweth S, Oh JK; U.S. CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med*. 2014;370:1790-8.
6. Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Sondergaard L, Mumtaz M, Adams DH, Deeb GM, Maini B, Gada H, Chetcuti S, Gleason T, Heiser J, Lange R, Merhi W, Oh JK, Olsen PS, Piazza N, Williams M, Windecker S, Yakubov SJ, Grube E, Makkar R, Lee JS, Conte J, Vang E, Nguyen H, Chang Y, Mugglin AS, Serruys PW, Kappetein AP; SURTAVI Investigators. Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients. *N Engl J Med*. 2017;376:1321-31.
7. Popma JJ, Deeb GM, Yakubov SJ, Mumtaz M, Gada H, O'Hair D, Bajwa T, Heiser JC, Merhi W, Kleiman NS, Askew J, Sorajja P, Rovin J, Chetcuti SJ, Adams DH, Teirstein PS, Zorn GL 3rd, Forrest JK, Tchétché D, Resar J, Walton A, Piazza N, Ramlawi B, Robinson N, Petrossian G, Gleason TG, Oh JK, Boulware MJ, Qiao H, Mugglin AS, Reardon MJ; Evolut Low Risk Trial Investigators. Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients. *N Engl J Med*. 2019;380:1706-15.
8. Cribier A, Eltchaninoff H, Bash A, Borenstein N, Tron C, Bauer F, Derumeaux G, Anselme F, Laborde F, Leon MB. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. *Circulation*. 2002;106:3006-8.
9. Thomas M, Schymik G, Walther T, Himbert D, Lefèvre T, Treede H, Eggebrecht H, Rubino P, Mischev I, Lange R, Anderson WN, Wendler O. Thirty-day results of the SAPIEN aortic Bioprosthesis European Outcome (SOURCE) Registry: A European registry of transcatheter aortic valve implantation using the Edwards SAPIEN valve. *Circulation*. 2010;122:62-9.
10. Schymik G, Lefèvre T, Bartorelli AL, Rubino P, Treede H, Walther T, Baumgartner H, Windecker S, Wendler O, Urban P, Mandinov L, Thomas M, Vahanian A. European experience with the second-generation Edwards SAPIEN XT transcatheter heart valve in patients with severe aortic stenosis: 1-year outcomes from the SOURCE XT Registry. *JACC Cardiovasc Interv*. 2015;8:657-69.
11. Wendler O, Schymik G, Treede H, Baumgartner H, Dumonteil N, Ihlberg L, Neumann FJ, Tarantini G, Zamarano JL, Vahanian A. SOURCE 3 Registry: Design and 30-Day Results of the European Postapproval Registry of the Latest Generation of the SAPIEN 3 Transcatheter Heart Valve. *Circulation*. 2017;135:1123-32.
12. Roques F, Nashef SA, Michel P, Gauducheau E, de Vincentiis C, Baudet E, Cortina J, David M, Faichney A, Gabrielle F, Gams E, Harjula A, Jones MT,

Pintor PP, Salamon R, Thulin L. Risk factors and outcome in European cardiac surgery: analysis of the EuroSCORE multinational database of 19030 patients. *Eur J Cardiothorac Surg*. 1999;15:816-22.

13. Dewey TM, Brown D, Ryan WH, Herbert MA, Prince SL, Mack MJ. Reliability of risk algorithms in predicting early and late operative outcomes in high-risk patients undergoing aortic valve replacement. *J Thorac Cardiovasc Surg*. 2008;135:180-7.

14. Kappetein AP, Head SJ, Génèreux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodés-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *Eur Heart J*. 2012;33:2403-18.

15. Waksman R, Rogers T, Torguson R, Gordon P, Ehsan A, Wilson SR, Goncalves J, Levitt R, Hahn C, Parikh P, Bilfinger T, Butzel D, Buchanan S, Hanna N, Garrett R, Asch F, Weissman G, Ben-Dor I, Shults C, Bastian R, Craig PE, Garcia-Garcia HM, Kolm P, Zou Q, Satler LF, Corso PJ. Transcatheter Aortic Valve Replacement in Low-Risk Patients With Symptomatic Severe Aortic Stenosis. *J Am Coll Cardiol*. 2018;72:2095-105.

16. <https://www.fda.gov/medical-devices/medical-device-recalls/2019-medical-device-recalls>. Last accessed on 26 September 2019.

17. Thourani VH, Kodali S, Makkar RR, Herrmann HC, Williams M, Babaliaros V, Smalling R, Lim S, Malaisrie SC, Kapadia S, Szeto WY, Greason KL, Kereiakes D, Ailawadi G, Whisenant BK, Devireddy C, Leipsic J, Hahn RT, Pibarot P, Weissman NJ, Jaber WA, Cohen DJ, Suri R, Tuzcu EM, Svensson LG, Webb JG, Moses JW, Mack MJ, Miller DC, Smith CR, Alu MC, Parvataneni R, D'Agostino RB Jr, Leon MB. Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis. *Lancet*. 2016;387:2218-25.

Supplementary data

Supplementary Table 1. Baseline characteristics.

Supplementary Table 2. In-hospital and 30-day outcomes.

The supplementary data are published online at:

<https://eurointervention.pcronline.com/>

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Supplementary data

Supplementary Table 1. Univariate and multivariate analysis of association between myocardial bridging and epicardial endothelial dysfunction.

	Odds ratio for mid and/or distal epicardial endothelial dysfunction	Confidence interval	<i>p</i>-value
N=591			
Univariate analysis			
Mid and/or distal vessel myocardial bridging	1.50	1.09 – 2.06	0.012*
Multivariate analysis*			
Mid and/or distal vessel myocardial bridging	1.44	1.04 – 2.00	0.029*
Age (per increase in age by 1 year)	0.99	0.98 – 1.00	0.068
Male sex	1.64	1.30 – 2.09	<0.001*
Current smoker			
(vs never smoker)	1.24	0.85 – 1.81	0.261
(vs former smoker)	1.37	0.93 – 2.03	0.112
Hypertension	0.90	0.71 – 1.15	0.417
Diabetes mellitus	0.89	0.59 – 1.32	0.550
Hyperlipidaemia	1.26	1.00 – 1.60	0.054
History of vascular disease	1.13	0.74 – 1.72	0.574

* Multivariate analysis adjusted for age, sex, smoking status, hypertension, diabetes mellitus, hyperlipidaemia, and vascular disease.

Supplementary Table 2. Univariate and multivariate analysis of association between myocardial bridging and microvascular endothelial dysfunction.

N=763	Odds ratio for microvascular endothelial dysfunction	Confidence interval	p-value
Univariate analysis			
Myocardial bridging	1.31	0.97 – 1.76	0.075
Multivariate analysis*			
Myocardial bridging	1.34	1.00 – 1.82	0.050*
Age (per increase in age by 1 year)	0.98	0.98 – 0.99	0.001*
Male sex	1.24	0.99 – 1.55	0.063
Current smoker			
(vs never smoker)	0.58	0.41 – 0.82	0.002*
(vs former smoker)	0.77	0.54 – 1.09	0.141
Hypertension	1.00	0.79 – 1.26	0.99
Diabetes mellitus	1.42	0.97 – 2.07	0.073
Hyperlipidaemia	0.94	0.75 – 1.18	0.618
History of vascular disease	1.01	0.68 – 1.49	0.972

* Multivariate analysis adjusted for age, sex, smoking status, hypertension, diabetes mellitus, hyperlipidaemia, and vascular disease.